(UCRL-10683 Suppl.)
Supplement

22p.

1611755

UNIVERSITY OF CALIFORNIA U. Berkeley
(2) Lawrence Radiation Laboratory
Berkeley, California

[2] (NASA Cont. R- 41; Contract No. W-7405-eng-48*)

N63 23017 NSG 94

(NASA CR-51998)

CODE-1

UNPUBLISHED PRELIMINARY DATA

SUPPLEMENT TO
BIOLOGY AND MEDICINE SEMIANNUAL REPORT,
Fall 1962

~~Fall 1962~~

Cornelius A. Tobias et al. 1962 (cop)

SPACE RADIATION STUDIES

NASA-AEC Research Group
Donner Laboratory

OTS PRICE

XEROX $ 2.60 ph
MICROFILM $ 0.86 mf.

*These studies are funded by the National Aeronautics and Space Administration through the Atomic Energy Commission and the Lawrence Radiation Laboratory.

Contents

INTRODUCTION

Cornelius A. Tobias

In the current period the preparation of radiation facilities specially designed for expansion of heavy-ion studies has gone ahead well; all the components of the new biomedical irradiation room, including the focusing devices for the beam, are ready and construction work is in progress. We expect to have the new shielded room ready and in operation early in September of 1963. We expect to be able to give omnidirectional proton irradiation to large mammals beginning sometime in October or November 1963. At the 88-inch cyclotron 120-MeV α particles were obtained and 65-MeV particles have been deflected. A biomedical shielded exposure area has been installed and several experiments have been carried out with the α-particle beam. This beam will have a variable penetration range up to about 1 cm in tissue and will be used in skin and brain studies with α particles and in brain studies for up to 3-cm penetration with protons. An abstract of a report by Graeme Welch on the progress is attached. (A-1)

The high-energy proton irradiation of animals with simulated flare spectrum involves experimental theoretical studies on the scattering and absorption of high-energy protons. We include two abstracts on the characteristics of a scattered proton beam in a thick target and on the pattern of depth dose distribution in a spherical phantom. (A-2 and A-3)

Calibration studies for high energy-charged particles were made on the dose response of glass, thermoluminescent and film dosimeters. These dosimeters will not only be used in the omnidirectional proton irradiation facility in our Laboratory but also may be useful in actual space flight when radiation dose is considered. (A-4) In this study we collaborated with E. Tochilin of the Naval Radiological Defense Laboratory in San Francisco.

Detailed studies on the mechanism and dose response of radiation effect from 730-MeV protons are being made at the cyclotron by Ashikawa, Sondhaus, and associates. It is very clear now that the high-energy protons produce a lethal effect primarily by visceral effects and not by bone-marrow effects. This is due to the relative lack of absorption of the protons in the bone. (A-6) We are also finding striking dose-rate dependence of the acute radiation syndrome in mice. (A-5)

Experiments that were performed last year during the Ames NASA balloon flight from Labrador have now been fully evaluated. We have obtained a total of 6% developmental abnormalities from irradiation of corn seeds. We were unable to produce similar abnormalities in the same seeds following radiation up to 3,000 r with x rays or to 40,000 rads with α particles in the Laboratory. (A-7)

What may be a potentially important effect was discovered in the laboratory by Mr. Nabil Amer on the modification of radiation injury with magnetic fields. Briefly, the presence of constant magnetic field cut down the wing developmental abnormalities in the beetle, *Tribolium confusum*, and causes a temperature dependence. (A-8)

Much work was done on the basic mechanism of radiation effect on microorganisms with heavily ionizing particles. We extended previous knowledge of x-ray effects on diploid yeast cells which indicated that in distilled water they will recover from a big part of the radiation injury following x irradiation. We now find recovery from heavy-ion damage in distilled water in diploid yeast cells but not in haploid yeast cells. This work was done by Lyman, Haynes, and associates. (A-9) The second demonstration from this Laboratory is that the effects of heavily ionizing beams in aqueous systems can be modified. A year and a half ago we demonstrated that glycerol profoundly modifies radiosensitivity to heavy ions.

Dr. Aldo Rescigno is making a somewhat new interpretation of radiation survival curves in terms of the theory of compartments. (A-10) Moreover, additional work was initiated on the effects of heavy ions on dried enzymes at extremely low temperature, and collaborated work is being carried out on the effects of heavy ions on bacterial spores.

In the realm of the physical chemistry of weightlessness, we believe we are making definite progress in understanding some qualitative and quantitative aspects of the weightless state. Dr. Howard Mel in our Laboratory has demonstrated a new effect — "streaming droplet sedimentation" — which is under the control of normal gravity. Briefly, the effect amounts to a diffusion-induced microconvectional instability at an initially stable boundary in his STAFLO liquid-flow system. This leads to a rapid transport process which can be used to control an enzymatic reaction in a manner that could not be brought about by ordinary diffusion alone. (A-11)

Dr. Milton Polissar is making a study of the flow of liquids that differ only very slightly in density or pH. He believes that this situation is analogous to what may occur in space flight when the g force is very low, since a small difference in density produces a small differential force on the elements of the liquid. By using color indicators he was able to study the behavior of fluids and their mixing properties at ground level, and quantitatively study these properties in situations that correspond to very low g. (A-12)

A-1. PROGRESS REPORT ON INSTRUMENTATION FOR BIOLOGICAL RESEARCH AT THE 88-INCH CYCLOTRON

Graeme Welch

Introduction

The 88-inch spiral-ridge cyclotron is designed to deliver protons at a maximum energy of 50 MeV, deuterons at 60 MeV, and α particles at 120 MeV, with an average beam current into the cave of 10 μA. Carbon, oxygen, nitrogen, and neon beams are also in the plans. Beam development has progressed to the stage where useful proton, deuteron, and α-particle beams of 40, 32, and 65 MeV, respectively, have been obtained for physical measurements.

Facilities and Instrumentation

To pursue biological work at the 88-inch cyclotron, several facilities, in addition to those already provided for chemistry and physics, have been designed and built. These include (a) a cave, (b) quadrupole magnet and power supply, (c) animal preparation room, (d) cave equipment, (e) electronic equipment, and (f) cyclotron pulse equipment.

Results as of 1 June 1963

Preliminary physical measurements of particle number vs distance and Bragg ionization-peak curves have been made on 40-MeV protons, 32-MeV deuterons, and 65-MeV α particles. For the protons the ratio of peak ionization to that of the full-energy particles is 5.2 to 1.

One biological experiment has been run as a follow-up of observed mutations in corn seeds due to cosmic rays at 40 km altitude and 2 days' exposure (balloon flight, July 1962). One-hundred-twenty corn seeds were exposed at the cyclotron to various doses of 40-MeV protons from 10,000 rads to 200,000 rads. The seeds are now germinating and the results will be known in a few months.

The reliability of cyclotron operation is improving, and the program of animal irradiations is expected to proceed shortly.

A-2. CHARACTERISTICS AND INTENSITY PROFILE OF A HIGH-ENERGY PROTON BEAM AFTER SCATTERING IN A THICK TARGET

Roger W. Wallace, Kenneth Kase, and Charles A. Sondhaus

Total body irradiation of large animals is presently impractical with the narrow strongly focused proton beam of the 184-inch cyclotron. Attempts have been made to scan large animals by sweeping the exposure holder uniformly through the beam, but mechanical difficulties and stress to the animal have made the technique impractical. To produce a total-body irradiation of a large animal without scanning, the first requirement is to enlarge the beam diameter until it exceeds the dimensions of the animal. If an omnidirectional exposure is required to simulate solar-flare proton-exposure geometry, an additional requirement is to present equal portions of the body surface to the beam for equal times at all possible angles by rotating the animal within the broad beam.

Scattering the beam rather than magnetic deflection has been selected as the method of choice for producing angular divergence. Based on the known properties of multiple Coulomb scattering, calculations have been made that predict the angular distribution of the emergent primary proton flux after passage through a scattering target. Substances considered as scatterers include lead, copper, aluminum, and graphite, and the energy range 1000 to 10 MeV has been investigated.

An angular divergence is predicted in the emergent beam which increases with target thickness and is greatest in the heaviest material for a given fraction of particle range. At the same time the intensity of the emergent primary beam within a given small solid angle is reduced because of nuclear interactions that result in secondary particles--mostly protons but including neutrons and mesons--the majority of which are scattered through somewhat larger angles than are the bulk of the multiply scattered primary protons. The resulting reduction in intensity is found to be greatest for the lightest material.

A second effect of the scattering process that has been investigated is the reduction in energy of the emerging particles. The degree of energy degradation for any material is dependent on the fraction of the proton range traversed in the target; this requires a greater thickness of light than of heavy material. Since angular dispersion of the beam is also a function of target thickness, it is evident that neither can be produced without the other. Thus a beam of angular divergence sufficient to irradiate a whole large animal will necessarily consist of lower-energy protons than did the incident beam before striking the target; similarly, a lower-energy beam cannot be used without introducing angular spread and resultant lower intensity. In addition, an energy spread will be produced in the emergent primary beam that will increase with target thickness; this energy straggling, however, remains a small percent of the emergent energy until very low degraded energies are reached, about 10 to 50 MeV, at which region it becomes comparable to the average energy of the emergent beam.

These calculations allow predictions to be made of the energy and intensity profile of the primary beam emerging from targets of each of the above materials. It appears that intensity can be made sensibly uniform over a circular area of radius greater than 15 cm at a distance of about 2 m from the scattering-target exit port. This distribution will result if a graphite target is used with thickness great enough to degrade the initial energy of 730 MeV to roughly 400 MeV. The resulting primary flux intensity appears to be reduced by a factor of about 100 to 1000, suggesting that the maximum dose rate achievable in air in the target region may lie in the range of 10 to 100 rads/min.

If a lower-energy beam is produced, it appears that the same area of roughly uniform intensity can be found at a much shorter distance from a copper target, and dose rate due to the primary beam may be kept to about the same value as above. It thus appears from the calculations that the stepwise simulation of a lethal solar-flare exposure by successive exposures at different proton energies may be time-consuming.

Since secondary-particle production also occurs in the scattering target and some fraction of the secondary-particle flux will also reach the animal, calculations are under way to estimate the increase in dose due to this component. The theory predicts that the secondary-particle flux will be smallest in graphite.

Finally, the feasibility of using a simple solid-state detector-absorber array, the output of which is fed into a coincidence counting and pulse-height-analyzing circuit, is being investigated as a means of obtaining particle identity and energy-distribution information on the emergent beam.

A-3. THE PATTERN OF DEPTH DOSE IN A SPHERICAL PHANTOM IRRADIATED OMNIDIRECTIONALLY WITH HIGH-ENERGY PROTONS

Charles A. Sondhaus, Palmer Steward, and Roger W. Wallace

In evaluating the effect of a total body exposure of a large animal to a proton flux, it is of considerable importance to know the distribution of tissue dose and of LET at various depths in the animal. Although both quantities appear to be essentially constant at all points in even a large animal when the proton energy is sufficiently high, two factors may produce deviations from uniformity. The first is the attenuation of the primary beam and the production of secondary particles by the interaction of primary protons with nuclei of atoms in the tissue. The second is the scattering and energy degradation of the primary proton flux by multiple Coulomb interactions in passage through the material. The relative importance of each process varies with the energy of the incident proton flux as well as with the size of the animal.

A number of calculations have been made by different investigators in attempting to predict the behavior of dose and LET with depth for the case in which the proton flux is distributed in energy and is isotropically incident, since present information indicates that these are the conditions under which an exposure to a solar-flare proton flux might occur during the course of a space flight. The numerical values of dose and the shapes of the depth-dose profiles resulting from such estimates differ somewhat according to the varying assumptions made in each investigation; the problem is a complex one, and detailed information on nuclear interactions and secondary-particle production is scarce. Furthermore, the energy spectrum of the solar-flare proton flux appears to vary greatly among different events and at different times during a given event, making the predicted values arbitrary to a certain extent.

In an effort to study this problem experimentally, lucite phantoms will be exposed to the proton beam of the 184-inch cyclotron after it has passed through a scattering target which produces energy degradation and angular divergence in the emergent broad beam. Dose will be measured at a series of radial depths inward from the surface of a test sphere and in tissue-equivalent animal phantoms by means of fluorescence readings in silver-activated phosphate-glass rod dosimeters as well as with lithium fluoride thermoluminescent dosimeters.

As a preliminary phase of these experiments, a series of calculations has been programmed for the 7090 computer at Lawrence Radiation Laboratory to predict approximately the dose, particle energy, and LET distribution in an omnidirectionally irradiated spherical phantom as a function of incident primary-particle energy and of sphere diameter. The program was designed to allow the input of any chosen value for each of the parameters involved so that improvement resulting from further experimental determinations may easily be incorporated into the computations.

The program of computation was divided into two parts. The first was the calculation of dose at given depth due to the primary proton flux alone.

Geometric differences in path length with angle of entry through a sphere lead to a distribution of energy in the primary proton flux arriving at each dose point. The percent of total dose contributed by protons in each of several energy intervals has therefore been tabulated, and the sum of the partial doses then forms the total dose due to the primaries. A value of dE/dx and thus of LET can be assigned to each energy, resulting in an average LET distribution at each point.

The second part of the computation was an approximate calculation of dose at each point due to two classes of interactions producing secondary particles: the nuclear cascade and the evaporation event. By assuming rough energy distributions for each and by carrying the cascade secondaries through successive depths, a total additional dose due to both at each depth point chosen can also be roughly broken down into energy intervals and added to the primary dose distribution. Meson and neutron doses were not considered in the present program.

The formulas that have been developed involve fitting the range-energy curve of protons in tissue to power functions of energy, five such functions being used to represent the range-energy relation over the energy region 0 to 1000 MeV. Five additional power functions are also used to represent the inelastic-scattering cross section in the same energy range. The effect of straggling is neglected for the primary beam; it is assumed further that all cascade secondaries are emitted in the forward direction-- a reasonable approximation for omnidirectional geometry. Only first-generation cascade secondary protons are included in the calculation, and only their ionization loss is considered. For the evaporation secondary protons, the assumption is made that their number is equal to the incident flux at each depth in the tissue, and that all their energy is deposited essentially at the point of formation; only first-generation evaporation secondaries are included. The energy spectrum of the cascade secondaries is assumed to be a power function, and that of the evaporation protons a Maxwellian distribution of low energy.

The output of the computer program is in the form of depth-dose data and fraction of dose due to each of several energy intervals at each dose point in the sphere; average LET distribution is calculable from the latter at each depth. These data have been calculated for spheres of diameter 5 to 100 cm, exposed omnidirectionally to monoenergetic proton fluxes of energy between 20 and 730 MeV. The curves of depth dose are essentially flat down to about 200 MeV, indicating that uniform whole-body exposure of large animals is possible at higher energies. Below this energy region the ratio of surface to midline dose increases rapidly with decreasing energy and increasing sphere diameter to values exceeding 100 at the lowest energies considered.

The dose distribution in a sphere exposed to a solar spectrum may thus be obtained by summing the contributions from each energy interval in an assumed spectral distribution. By reproducing experimentally the dose distribution predicted for a test sphere, the proper exposure times and proton energies can be chosen to simulate the solar-flare condition to a degree sufficient for animal irradiation. A large animal rotator has been constructed for use in the large-animal total-body omnidirectional exposures, and the experimental dose determinations will be made with the phantom or test sphere placed within it.

A-4. THE DOSE RESPONSE OF GLASS, THERMOLUMINESCENT, AND FILM DOSIMETERS TO HIGH-ENERGY CHARGED PARTICLES*

Eugene Tochilin, John T. Lyman, Frank H. Attix, and E. J. West

The wide linear dose range, good storage characteristics, and small size of certain solid-state dosimeters has led to their use in measuring radiation fields encountered during space flights. Although extensive information is available on the behavior of these systems to electrons and γ rays, there are virtually no data on their response to protons and other heavy cosmic-ray particles. The measurements made with 900-MeV α particles at the Lawrence Radiation Laboratory 184-inch cyclotron constitute an initial attempt to obtain such information on a specific group of detectors.

A study was made on the response of silver-activated phosphate glass dosimeters and of CaF_2:Mn and LiF thermoluminescence dosimeters to the primary α-particle beam and at various points along the Bragg curve. The initial experiment was carried out by placing the glass dosimeters at different depths in a rectangular Lucite block approx 5 cm square and 30 cm long. The block consisted of individual sections between which the dosimeters were positioned. Each dosimeter was 1 mm in diameter and 6 mm long. The entire array of dosimeters was housed in a cavity in a Lucite chip 2×2 cm square and 1.5-mm thick. Prior to the dosimeter run, an experiment was conducted with Eastman Type KK and DuPont Type 555 and Type 834 films. This served to determine beam alignment, uniformity of beam, and the overall dose response of film throughout the range of the particle beam. The films were later placed directly behind each dosimeter chip as a check on beam alignment during the run. Type 834 emulsion was virtually the same as that reported in an earlier study at the cyclotron with 300-MeV protons.[1] The Eastman KK and DuPont 555 emulsions, which are the most sensitive films available, were found to be esentially flux detectors in this region. They were used as monitors to determine the loss in particle flux of the alpha beam passing through the Lucite absorber block. Results obtained with the glass dosimeters proved disappointing. This was due to two complicating effects. Firstly, there was a marked density difference between the individual glass rods. Since these were aligned one behind the other in the block, the effective particle range was different for each system. This made any determination of the rate of energy loss with depth difficult. Secondly, a marked gradient was found to exist over the beam area subtended by the dosimeter chip. It was decided to repeat the experiment under more favorable conditions.

The second experimental run was carried out with measurements made behind absorbers of 0.25-, 1.6-, 2.0-, 2.10-, and 2.15-in. copper. Ionization-chamber measurements determined the relative ionization behind each absorber. Dosimeters were once again exposed in the Lucite chips

---

*This work was a joint effort of the Naval Radiological Defense Laboratory, San Francisco, the Naval Research Laboratory, Washington, D. C., and Donner Laboratory, Berkeley.

[1] E. Tochilin, B. W. Shumway, and G. D. Kohler, Response of Photographic Emulsions to Charged Particles and Neutrons, Radiation Res. **4**, 467 (1956).

previously described, with photographic emulsions placed behind each chip to determine beam uniformity. Dosimeters were exposed behind all five absorbers at dose rates of 200, 500, and 1000 rads per min. Additional exposures were made behind the 0.25-in. absorber at dose rates of 50 and 3200 rads per min. The three types of silver phosphate glass dosimeters gave similar results. The data are given in Table I. To summarize, the glasses have a 15% higher dosage sensitivity to 900-MeV α particles than to Co^{60} γ rays. This dosage sensitivity decreases with increasing dE/dx. At a rate of energy loss corresponding to 40 times minimum ionization (5 times the primary beam), the dosage sensitivity decreased by 50%. There was no apparent dose rate or dose dependence over the range investigated. The picture is less clear-cut for the thermoluminescent dosimeters. With CaF_2Mn there is an increase in dosage sensitivity relative to Co^{60} as the α dose is increased. The slope of the curve of α-particle dose vs apparent Co^{60} dose was 0.8. At 600 rads the dosage sensitivity is some 25% higher than that for Co^{60}. This suggests that the α particles are producing radiation damage that results in additional electron traps, which in turn produce increased sensitivity.

The LiF system produced even less-consistent results. Dosage sensitivity ranged from 0.4 to 0.7 over the region investigated, and it is possible that the data are complicated by the fact that these dosimeters were the same ones used for the earilier runs. The results may therefore, in part, reflect the results of previous radiation damage. One additional run with fresh dosimeters should help clarify this picture.

Table I. Dosage sensitivity of three silver phosphate glasses relative to Co^{60} absorbed dose.[a]

Manufacturer	Type of glass	Relative dosage sensitivity
B & L	High Z	1.15
B & L	Low Z	1.14
Toshiba	Low Z	1.12

[a]The dosage sensitivity is based on a comparison of absorbed dose in rads in the glass systems.

A-5. DIFFERENCE IN THE ACUTE RADIATION SYNDROME AND ITS DOSE-RATE DEPENDENCE FOR 100-kVp X RAYS AND 730-MeV PROTONS

James K. Ashikawa, Charles A. Sondhaus,
Cornelius A. Tobias, and Dave Love

Randomly bred, selected Male Swiss Webster white mice 6 to 7 weeks old and weighing 28 ± 3 g were exposed individually to the proton beam of the 184-inch cyclotron. In a series of 4 experiments, the time course of radiation mortality was followed in more than 700 total-body irradiated animals. An equal number of randomized litter-mate animals were similarly exposed to 100-kVp x radiation filtered by 1.0-mm Al. The exposures were made in individual plastic holders, dorsoventrally in the x-ray beam and anteroposteriorly in the proton beam. Proton exposures were made at 100, 300, and 1000 rads/min, while x-ray exposures were made at 20 and 100 rads/min, midline air dose. The midline air dose varied from 500 to 1100 rads per exposure. All animals were individually caged in glass jars from 2 weeks preirradiation until the end of each experiment. Only animals showing weight gain during the 2 weeks of caging for preirradiation isolation and acclimatizing were selected for the experiments.

In the proton-irradiated animals, peak mortality occurred at 4 to 6 days postirradiation at all doses in the 30-day lethal range. Previous work at this and other laboratories has shown that in the mouse death during this period is due predominantly to gastrointestinal injury. In animals irradiated with 30-day lethal doses of x rays, on the other hand, peak mortality occurred at 12 to 14 days postirradiation, which is known to indicate that death was due mainly to loss of hematopoetic function.

Animals receiving a proton dose at 1000 rads/min exhibited a marked increase in incidence and abruptness of 4 to 6-day gut deaths over those irradiated at 100 rads/min, although the 30-day mortality was the same in both groups for a given total dose. Thus, at 5 days, 30% mortality was observed in the animals irradiated at 100 rads/min, whereas 60% mortality had already been reached in the animals irradiated at 1000 rads/min. For animals irradiated at 300 rads/min, an intermediate effect was observed.

In animals x irradiated with 30-day lethal doses, a fivefold increase in dose rate from 20 to 100 rads/min produced few deaths from the gut syndrome, but the higher dose rate did effect a similar enhancement of the marrow syndrome. When a larger total x-ray dose was given, however -- high enough to produce 100% lethality in 12 days -- the dose-rate effect on gut death was again observed. In the latter case, 5% 6-day deaths were observed at 20 rads/min while 20% 6-day deaths were seen at 100 rads/min of 100-kVp x ray. Since a dose rate higher than 100 rads/min was unobtainable with 100-kVp x rays, the effect of 1000 rads/min could not be investigated.

Since the LET spectrum for 100-kVp x rays does not differ greatly from that of 730-MeV protons, the marked difference observed in mode of death must be due to the difference in tissue dose distribution in gut and bone marrow between the two radiations. In the high-energy proton exposure, dose is uniform and thus comparable in both organs, and has a constant relation to air dose. In exposure to soft x rays, calculation has shown that local dose in the marrow cavities may reach several times the average air dose, while the decrease in tissue dose with depth in turn lowers the gut dose relative to air dose.

It thus becomes difficult to observe a bone-marrow death with high-energy protons, because the rapidly occurring gut syndrome will supervene first if a uniform dose high enough to produce either mode of death is given. With soft x rays, on the other hand, either the high ratio of bone marrow dose to gut dose or the greater radiosensitivity of the marrow causes the marrow death to appear first.

Each syndrome in turn is subject to a dose-rate effect; this appears in the gut syndrome with protons, and can be made to appear in either syndrome with x rays. If the total air dose is made high enough with soft x rays to produce gut death soon after irradiation, the dose-rate dependency of gut death is seen. If the total air dose is not high enough to produce gut death, either the high local marrow dose or the high marrow radiosensitivity produces marrow death, which also exhibits dose-rate dependency.

By protecting the proton-irradiated animal against gut death, it should be possible to produce the marrow syndrome and to demonstrate its dose-rate dependence with protons. It should then also be possible to determine what proton dose to the bone marrow is required to produce the syndrome, and thus to investigate the relative radiosensitivity of the bone marrow.

A-6. SOME FACTORS INFLUENCING RBE OF HIGH ENERGY PROTONS

Charles A. Sondhaus, James K. Ashikawa,
Cornelius A. Tobias, and Vally Paschkes

In a series of seven experiments with 730-MeV protons, 100-kVp and 250-kVp x radiation, the relative lethality and time course of radiation injury was studied in more than 2000 Swiss Webster white mice. Experimental conditions and differences observed in the radiation syndrome are described in the previous abstract (5).

It is well known that the type and degree of biological effect from a given radiation exposure depends on a number of factors in addition to absorbed dose. Differences in the predominance of the gastrointestinal and hematopoetic syndromes at different total doses and dose rates for each radiation make it necessary to include the effect of these factors and to specify the mode of injury for comparison of the effectiveness of high-energy protons and x radiation.

Since gut and marrow deaths occur at distinct and well separated times after lethal total-body irradiation in mice, these animals were chosen for the study. The characteristic times of peak death rate for each injury mode suggested that 6-day and 12-day mortality be selected as end points for comparison, in addition to the more usual 30-day median lethal dose (LD_{50}). These quantities were therefore determined for different total doses of all three radiations at constant dose rate. The effect of varying the dose rate was also studied.

The values summarized below are approximate and are based on a preliminary analysis of cumulative mortality data.

For 730-MeV protons, the 30-day total-body LD_{50} was found to be 650 rads air dose. This value was not significantly different at dose rates of 1000, 300, and 100 rads/min. The 12-day LD_{50} values, however, were 680 rads at 1000 rads/min and 700 rads at 100 rads/min, and the 6-day LD_{50} was 730 rads and 810 rads respectively, at the two dose rates.

For 250-kVp x radiation filtered with 0.5 mm Cu + 1.0 mm Al, the 30-day total-body LD_{50} was 520 rads air dose for dose rates of both 100 rads/min and 20 rads/min. The 12-day LD_{50} was 610 and 630 rads respectively, and the 6-day LD_{50} was about 1000 rad at 100 rad/min; the 6-day LD_{50} at 20 rad/min is being investigated.

For 100-kVp x radiation filtered with 1.0-mm Al, the 30-day total-body LD_{50} was 750 rads, midline air dose, for dose rates of both 100 rads/min and 20 rads/min. The 12-day LD_{50} was 850 and 900 rads respectively, while the 6-day LD_{50} levels were not reached at the total doses given but could be estimated as greater than 1100 rads at 100 rads/min and greater than 1300 rads at 20 rads/min.

Based on these data, tentative estimates of proton RBE (relative biological effectiveness) may be made for gut death as well as for 30-day LD_{50}. If 30-day LD_{50} is used as end point, a value of 0.8 is found for 730-MeV protons, which agrees well with previous results obtained at this Laboratory and elsewhere. On the other hand, if gut death is used as end point, a different RBE results and dose rate is found to influence it. The 6-day RBE for protons at 1000 rads/min relative to 250-kVp x ray at 100 rads/min is the highest observed, a value of 1.4 being found. For protons at 100 rads/min, however, the 6-day RBE was 1.2 if the 250-kVp x irradiation was made at the same dose rate.

The higher but variable RBE at 6-day LD_{50} level appears to be due to two factors. The first is the difference in tissue dose distribution between the two radiations, which favors the production of gut death by high-energy proton exposure. The second is the dose-rate dependency of the syndrome.

The 100-kVp x radiation is particularly efficient in producing marrow death but causes gut death only at high air doses. Thus, a midline air dose more than 1.3 times that for 730-MeV protons was required to produce 50% gut death at 6 days, although 0.9 times the proton air dose produced the same LD_{50} at 30 days. To derive a true ratio of marrow doses, however, the average value of dose in the microscopic marrow cavities for 100-kVp x ray would have to be obtained. Calculation has shown this dose to be several times as high in the smallest cavities as in the soft tissue surrounding the bone, but no average value can be assigned to the marrow as a whole at this time.

If the cumulative mortality at 8 days, for example, were subtracted from the cumulative mortality at 30 days, a rough measure of bone-marrow mortality might result for each radiation, since most gut deaths have occurred by this time and marrow injury has not yet manifested itself to any extent. If this is done for the proton exposures, very little mortality remains at later times, in contrast to the x-ray exposures, and much higher marrow RBE values would result for the remaining mortality. The poor statistics that would result make this procedure of doubtful significance with the present data. The use of larger numbers of animals together with protection against gut death would, however, make it possible to further investigate proton RBE for marrow.

A-7. EFFECTS OF COSMIC RADIATION ON SEED DIFFERENTIATION AND DEVELOPMENT*

John V. Slater and Cornelius A. Tobias

Seeds of a variety of plants were flown during the past year in co-operation with NASA by means of high-altitude balloons over Labrador. Nuclear emulsions accompanying the seeds showed the presence of approx 20 heavy ions per square centimeter with various atomic numbers up to and including that of iron. These flights lasted approx 50 h at an altitude of 25 miles. The effects, noticed mainly with corn (Golden bantam) and attributed to cosmic radiation, were

(a) arrests in pigmentation,
(b) irregular morphogenesis,
and (c) early cell loss resulting in visible streaks in the leaves.

Seeds of African daisies exhibited a lowered percentage of germination after the flights. Approximately 6% of the corn seeds flown exhibited some defect. It is expected that satellite flights of the seed material used may result in increased effects, especially if flown through radiation belts.

Research with the Berkeley Hilac is currently under way in attempts to evaluate the effects of heavy ions under controlled conditions at sea level on seed development and differentiation.

---

*Abstract of paper presented at the Eleventh Annual Meeting of the Radiation Research Society, Marquette University, Milwaukee, Wisconsin, May 26 to 20, 1963.

A-8. MODIFICATION OF RADIATION INJURY WITH MAGNETIC FIELDS*

Nabil M. Amer

Pupae of Tribolium confusum were irradiated with 1200 r of 250-kVp x rays. Following irradiation, one group of pupae was placed between the poles of a permanent magnet with a field of 3.6 kG. A second group was placed between the poles of a dummy magnet of the same geometry. Both groups were incubated at 38°C. After 7 days, the time necessary for the pupae to change to adults, the adults were studied in relation to induction of wing abnormality by following the methods of Beck, Slater, et al. The group incubated in the dummy magnet had a 93.4% ± 1.4 incidence of abnormal wing development. The group incubated in the magnetic field exhibited 54.1% ± 5.3 incidence of abnormal wing development. The remaining adults were normal; pupal death did not exceed 3% of the total number of pupae. The wing abnormality in the group exposed to the magnetic field was less intense than in abnormals of the control group. The experiment has been repeated four times with a total of 728 pupae.

These results show that the magnetic field at the strength indicated has a protective effect in modifying the radiation-induced damage in this system. A comparative study of free-radical content of the magneto-protected group vs the control group is being made. The possible influence of different magnetic-field intensities and the effect of time exposure to the magnetic field subsequent to irradiation are being investigated further.

---

*Abstract of paper presented at the Eleventh Annual Meeting of the Radiation Research Society, Marquette University, Milwaukee, Wisconsin, May 26 to 20, 1963.

A-9. RECOVERY OF YEAST FOLLOWING HEAVY-ION IRRADIATION*

John T. Lyman, Robert H. Haynes, and Cornelius A. Tobias

Following exposure of diploid yeast (Saccharomyces cerevisiae) to either x rays, ultraviolet light, or nitrogen mustard, a great increase in viability is observed if the irradiated cells are stored in distilled water (30°C) for 1 to 4 days before plating. The results of previous studies of this dark-recovery process by Patrick and Haynes (at the University of Chicago) are consistent with the view that these cells possess enzymes which, under appropriate conditions, are capable of modifying a significant fraction of those radiation-induced molecular lesions that would otherwise lead to cellular inactivation. It is of some interest to know whether or not such a recovery mechanism can operate in cells irradiated with heavy ions because it is not implausible to imagine that more severe local structural damage might be produced within the columns of dense ionization formed along the tracks of these particles. We have found that storage recovery can indeed occur in diploid yeast (strain X841) following irradiation by both carbon and neon ions with an energy of 10 MeV per nucleon. The recovery process appears to act as a constant dose-modifying agent over several decades of survival; the dose-modifying factor is approximately 2 for both ions, which is comparable to that observed for conventional x rays. Thus, the storage-recovery mechanism seems to function equally well in cells damaged by either high or low LET radiations.

---

*Abstract of paper presented at the Eleventh Annual Meeting of the Radiation Research Society, Marquette University, Milwaukee, Wisconsin, May 26 to 20, 1963.

A-10. INTERPRETATION OF THE MULTI-HIT CURVE IN TERMS OF THE THEORY OF COMPARTMENTS*

Aldo Rescigno

The equation $S = 1-(1-e^{-kD})^n$, where S is the standardized response to a dosage D, and k and n are positive constants, is compared with the equation $X = \Sigma_i A_i e^{-\alpha_i t}$, where X is the amount of a material in a certain compartment at a time t after the breaking of an essential connection between two precursor compartments. If certain conditions are imposed on the structure of a system of compartment, the two foregoing equations have the same form if one puts D = Rt and S = KX, where R and K are positive constants. Some physical interpretations are suggested for these two constants.

*Abstract of paper presented at the Eleventh Annual Meeting of the Radiation Research Society, Marquette University, Milwaukee, Wisconsin, May 26 to 29, 1963.

A-11. DIFFUSION-GRAVITY-CONTROLLED ENZYME-SUBSTRATE REACTION

Howard C. Mel

Competitive diffusion and the normal force of gravity interact to transport lysozyme rapidly into its separated substrate, in an initially stably layered, flowing system. In this manner, a continuous steady-state enzyme-substrate reaction is controlled by gravity and the diffusion coefficients of inert components. If this transport mechanism should play a role in any biological function, then in the "weightless" state the function would be altered or removed.

A-12. CONVECTION IN LOW GRAVITATIONAL FIELDS

Milton J. Polissar

Point sources of metabolic heat within a living cell tend to produce inequalities of temperature within the cell, with accompanying inequalities in density. Differences in molecular traffic across different parts of the boundary of the cell also tend to produce nonuniform density within the cell. The same tendency exists in larger cavities filled with liquid. Under terrestial conditions, steady state is maintained by diffusion, by movement of water across the boundary, and by gravitational convection. Convectional motion is absent under weightlessness and is reduced in low gravitational fields. The following questions are of biological interest: What may be the long-term effects of weightlessness or of reduced gravity upon the development and the behavior of a cell? What may be the effect upon larger biological entities if convection in some of their quiescent cavities is eliminated? The ultimate goal of the investigation reported here is to seek answers to these questions.

As a point of departure, convectional motion in macroscopic systems is being investigated. Specifically, answers are sought to the questions: Given a solution of density ρ, situated under a solution of density $\rho + \Delta\rho$, with the two solutions connected by a tube of radius R; what is the qualitative nature of the convectional exchange between the two solutions? How are the qualitative nature and the magnitude q of the volume-rate of convectional exchange between the two solutions affected by the magnitude of the gravitational acceleration g (here considered as variable)? In addition to the variables mentioned already, the magnitude of q is apt to be affected also by the effective viscosity η within the exchange tube and by the angle of inclination θ of the tube.

<u>Dimensional considerations</u> lead to the following conclusions:

$$F(q; \rho; \Delta\rho; R; \eta; \theta; g) = 0, \tag{1}$$

$$q = \frac{(g \cdot \Delta\rho)R^4}{\eta} \cdot f\left(\frac{g\rho}{\eta R}; \frac{\Delta\rho}{\rho}; \theta\right), \tag{2}$$

where f is a function of the two dimensionless products and of the angle θ.

For low speeds of exchange, where the changes in kinetic energy are small, Eq. (2) degenerates to the simpler expression

$$q = \text{constant} \cdot \left(\frac{(g \cdot \Delta\rho)R^4}{\eta}\right) \cdot f(\theta). \tag{3}$$

<u>Simulation of variation in g</u>

In Eq. (3) the quantities g and $\Delta\rho$ appear jointly, as a product. Variation in g may be simulated by an appropriate inverse change in $\Delta\rho$. In other words, it is possible to study the effects of changing g by changing the density difference between the two solutions.

Experimental procedures

The value of $\Delta\rho$ is controlled by loading the upper solution with sodium chloride. Quantitative measurements of q are made possible by adding a small amount of acid to one solution and a small amount of base to the second, and by titrating samples taken from the lower solution. Visual observation of the nature of the convectional motion is made possible by the addition of an acid-base indicator to both solutions.

Experimental Results

When the driving force is large and the exchange tube is vertical, the countercurrent movement through the exchange tube is highly turbulent. When the tube is inclined, the turbulent movement changes into a two-channel flow, with the lighter solution moving upward through the upper channel. When the driving force is low, movement through the exchange tube is laminar, even for $\theta = 0$, with two clearly visible channels.

When the driving force is not too high, the value of q is proportional to $\Delta\rho$ and to the fourth power of R, as predicted by Eq. (3).

When the value of $\Delta\rho$ is increased, in a series of experiments, the rate of exchange follows Eq. (3) over moderate changes in $\Delta\rho$. Eventually, with higher values of $\Delta\rho$, the rate deviates from proportionality, becoming smaller than predicted values. At still higher values of $\Delta\rho$, the rate passes through a maximum, then decreases, and eventually reaches a fairly constant value, independent of $\Delta\rho$. Visual observations show that the onset of this irregular behavior is associated with the onset of turbulence in the motion through the exchange tube.

When the rate is decreased in a series of experiments, by decreasing either $\Delta\rho$ or the radius of the tube, another irregularity appears: The value of q becomes much smaller than that predicted by Eq. (3). Not enough observations have so far been made to describe this irregularity in greater detail or to offer an explanation of this discrepancy. A study of this phenomenon is in progress. Clearly, extrapolation of the observations to microscopic systems must be postponed, pending the investigation of this phenomenon.

Qualitative and semiquantitative observations were also made on the following type of system: A cylindrical tube is filled with two aqueous solutions, with the heavier solution in the lower half of the tube. The tube is then rotated through an angle of 90 degrees in the vertical plane. When, in separate experiments, the value of $\Delta\rho$ is decreased by a factor of not more than 100, the behavior of each system may be described as approximately a slow-motion analog of the highest member of the series. The period of oscillation of the boundary about its equilibrium position is inversely proportional to the square root of $\Delta\rho$. The details of the manner of approach to equilibrium are too numerous to describe in this short report. A color film record of observations is available. When the value of $\Delta\rho$ is decreased still further, the whole nature of the convectional motion is changed.